

REMARKS/ARGUMENTS

Reconsideration of the Rejections and Objections of the Office Action and allowance of the claims are respectfully requested in view of Applicants' remarks below.

Remarks Regarding Claim Amendments

Applicants have amended claims 1-3, 5, 7-8, 17, 19 and 25 to correct typographical errors and to replace the word "impact" with "synergistic effect." Support for the amendments may be found throughout the Specification, such as, for example, on page 7, lines 1-3.

Claim 20 is marked "Previously Presented" to indicate the reversal of its former withdrawn status by the Examiner.

No new matter is added by the amendments and their entry is respectfully requested.

Remarks Regarding Section 103

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See *id.* ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order

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to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue“). The use of hindsight reasoning is impermissible. See *id.* at 1397 (“A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning”). Thus, a *prima facie* case under Section 103(a) requires “some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct.” *Kahn* at 1335; see *KSR* at 1396.

Claims 1-20, and 25 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over each of Huyn (U.S. Publication No. 2002/0095260), Borisy (U.S. Publication No. 2003/0096309), Afeyan (U.S. Publication No. 2005/0283320), Khwaja (U.S. Patent No. 6,379,714) and Pugh (J. Agricultural Food Chem. entitled “Characterization of Aloeride, A new High MW Polysaccharide form Aloe vera with Potent Immunostimulatory Activity”). Applicants traverse.

The present application provides a method to identify, within a complex multicomponent natural product, the components or groups of components and their respective concentrations which are required for producing a **synergistic effect** on the biological profile of a disease. The identification of these components provides a scientific basis for testing the efficacy and safety of complex natural products (see, e.g., page 7, lines 10-12 of Applicants’ Specification). The present invention, in contrast to the prior art, relates to the characterization of multiple components within a complex mixture using a multivariate analysis. Therefore, both the data input (product mixture) and the information extracted (biological profile) from the analysis is multifactorial in nature.

As argued in Applicants' previous response, none of the cited art documents relate to methods for determining components of a natural product having a synergistic effect on the complex biological profile of a disease. Borisy *et al.* describe a method of target-centric screening for drug-drug interactions using a library of synthetic or purified compounds. Huyn describes a biological marker identification method that can be used to assess response to a drug. Afeyan *et al.* relates to a method for profiling a biological system. None of these references relate to multicomponent natural products or to the problem of identifying components within said products that produce a synergistic effect.

Pugh *et al.* describe the effects of one component (Aloeride) of aloe gel in *in vitro* assays. Khwaja *et al.* describe methods for making pharmaceutical grade botanical materials, whereby the biological activity of the botanical material as a whole is assayed. These further references are also unrelated to the problem of identifying components within multicomponent natural products that produce a synergistic effect.

The Examiner states on page 4 of the Office Action that "most all drugs originated in natural products . . . and the desired activity was found in some fashion to be associated with a specific and **single** chemical . . ." (emphasis added). By contrast, the present invention is directed to identifying components of natural products that act **synergistically**.

The Examiner further states on page 4 of the Office action that "In other cases, such as in the references above, synergy between components was investigated". Applicants assume that the Examiner is referring to, for example, Borisy *et al.*, which describes effects from random combinations of isolated drugs. However, none of the cited documents suggests identifying sub-components of natural products that act synergistically. The present invention, in contrast to the

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cited references, is based on a holistic approach to develop new medicaments (see, e.g., Specification, page 2, lines 17-30).

Furthermore, the present invention finds bioactive compound profiles that work in synergy using a disease pattern. Other approaches use a single disease marker for a disease evaluation (reductionistic approach), whereas the present invention applies multifactorial disease patterns (systemic or holistic approach).

For the reasons stated above, withdrawal of the Section 103 rejections is requested because the claims would not have been obvious to one of ordinary skill in the art when this invention was made.

Remarks Regarding Section 112 First Paragraph

Claims 1-20 and 25 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Applicants traverse.

The disclosure in the application as filed clearly demonstrates that Applicants were in possession of the claimed invention at the time the application was filed. The Example described on pages 16-18 of the international publication describes a typical experiment of how to implement the claimed method. The Examiner states that the experiment is entirely hypothetical and no subject, disease, biomarker or multivariate analysis is shown. Applicants note, however, that an actual reduction to practice is not a requirement for patentability and is but one of many ways to demonstrate possession of the invention.

The application describes each step of the claimed method in such a fashion that one of skill in the art could practice the invention. The method itself, is not limited to a particular

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subject, disease, or biomarker, but rather, is useful for a number of analyses. Suitable subjects are described on page 6, lines 19-21; suitable diseases are any disease of which a biological profile can be determined (page 7, lines 7-9); suitable biomarkers are described on page 7, lines 19-30.

The Examiner further states that the “specification reveals no natural products, no improvements and no multivariate analysis” (see page 6 of Office Action). The application describes, however, natural products on page 6, lines 14-18 and page 10, lines 27-33. Multivariate analysis is described, for example, on page 14, line 19 to page 15, lines 15. With regard to “improvements”, Applicants submit that the application provides a method related to identifying components of natural products having synergistic effects. The Example on pages 18-19 describes how these components are identified by correlating data obtained from, for example, Figures 1, 2, and 3.

Withdrawal of the written description rejection made under Section 112, first paragraph, is requested because the specification conveys to a person skilled in the art that Applicants were in possession of the claimed invention as of the filing date. Their disclosure would also teach a skilled person, who possesses general knowledge available in the art, how to make and use the claimed invention.

Remarks Regarding Section 112 Second Paragraph

Claims 17, 19 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Applicants traverse.

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Applicants' traverse this rejection because one of ordinary skill in the art, upon reading Applicants' teaching in the instant Patent Application, would be able to understand with clarity the metes and bounds of claims 17 and 19.

Claim 17 is allegedly indefinite because of the use of parentheses. Solely in an effort to expedite prosecution, Applicants have amended claim 17 to remove all parentheses.

Claim 19 is allegedly indefinite because (1) "what the samples may be is not understood regarding the range" and (2) the claim lacks a period. With respect to point one, Applicants have amended the claim to more clearly define one aspect of the invention. With respect to point 2, Applicants thank the examiner for pointing out the typographical error. A period has been added to the claim.

This rejection is moot in view of Applicants' amendments. Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

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CONCLUSION

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

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